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Case Report

Deep vein thrombosis as thrombotic sequelae of vaccine-induced thrombotic thrombocytopenia

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Abstract

Administration of the ChAdOx1 nCoV-19 (AstraZeneca) vaccination has recently been associated with rare, unusual cases of thrombotic events. We report a case of a 55-year-old woman who presented to hospital with headaches, petechial rashes and bruising—7 days after receiving her first vaccine dose. Blood tests showed low platelets, a markedly high d-dimer and positive anti-platelet factor 4 antibodies. Computed tomography (CT) of head and venogram showed features consistent with venous sinus thrombosis. She was immediately started on IV pooled immunoglobulin therapy, high-dose prednisolone and full anticoagulation. Subsequent magnetic resonance imaging of head and venogram supported the initial CT findings, with features suggestive of a small-volume venous sinus thrombosis. Additionally, CT pulmonary angiogram revealed a right-sided segmental pulmonary embolism. Our case highlights the importance of increased awareness of this complication after covid vaccination and how searching for distal thrombotic events and liaison with tertiary centres influence clinical outcomes.

INTRODUCTION

The global outbreak of coronavirus disease, caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), prompted the development of several vaccinations to reduce the prevalence and serious adverse effects of the disease [1].

In February 2021, several cases of thrombotic events were noted after the administration of the ChAdOx1 nCoV-19 (AstraZeneca) vaccination—a recombinant chimpanzee adenoviral vector encoding the glycoprotein of SARS-CoV-2 [2].

The European Medicines Agency reported rare thrombocytopenia and thrombosis after receipt of the AstraZeneca vaccine [3]. In 72% of these cases, patients had developed cerebral venous sinus thrombosis (CVST) [3]. Although the presenting features were similar to heparin-induced thrombocytopenia, no prior exposure to heparin was noted; hence the diagnosis of vaccine-induced thrombotic thrombocytopenia (VITT) [2].

We report one such case of VITT and the importance of targeted imaging.

CASE REPORT

A 55-year-old female presented with a 7-day history of headache, visual disturbance, bilateral lower limb petechial rash and limb bruising; 2 weeks prior, she received her first dose of the AstraZeneca vaccine, developing symptoms 1 week later. She presented to her general practitioner (GP) who treated her for a urinary tract infection due to microscopic haematuria.

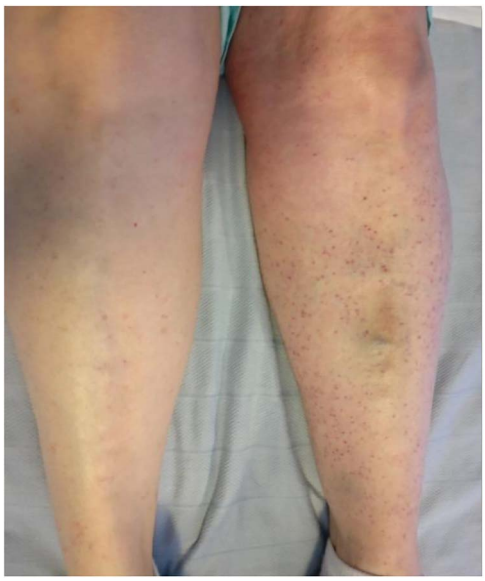

Figure 1. Petechial rash with peripheral bruising.

She represented to her GP 1 week later with persistent symptoms and a new rash on her lower legs (see Fig. 1). She was otherwise fit and well. Regular medications were ramipril and atorvastatin. She had hypertension. There was no personal or

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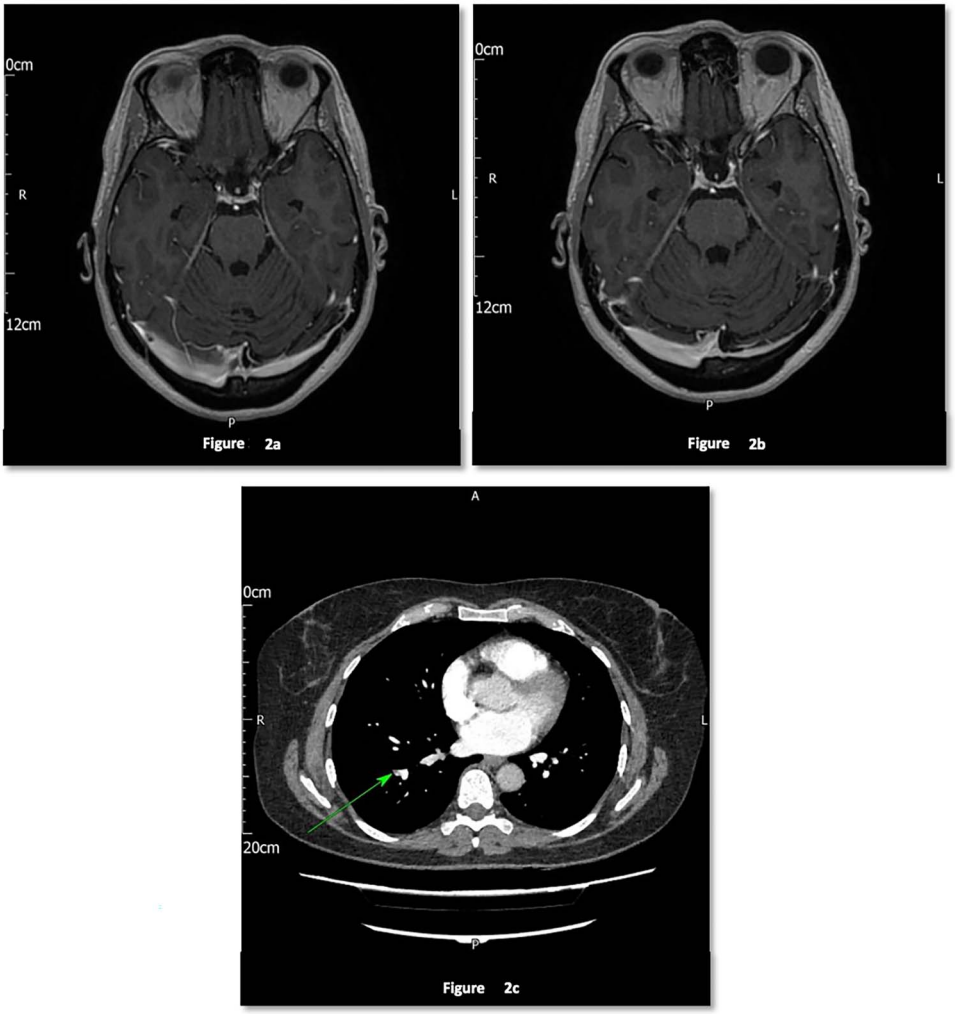

Figure 2. (**a**) MRI—dominant right transverse sinus, (**b**) MRI—filling defect in right transverse sinus and (**c**) CTPA showing subsegmental filling defects.

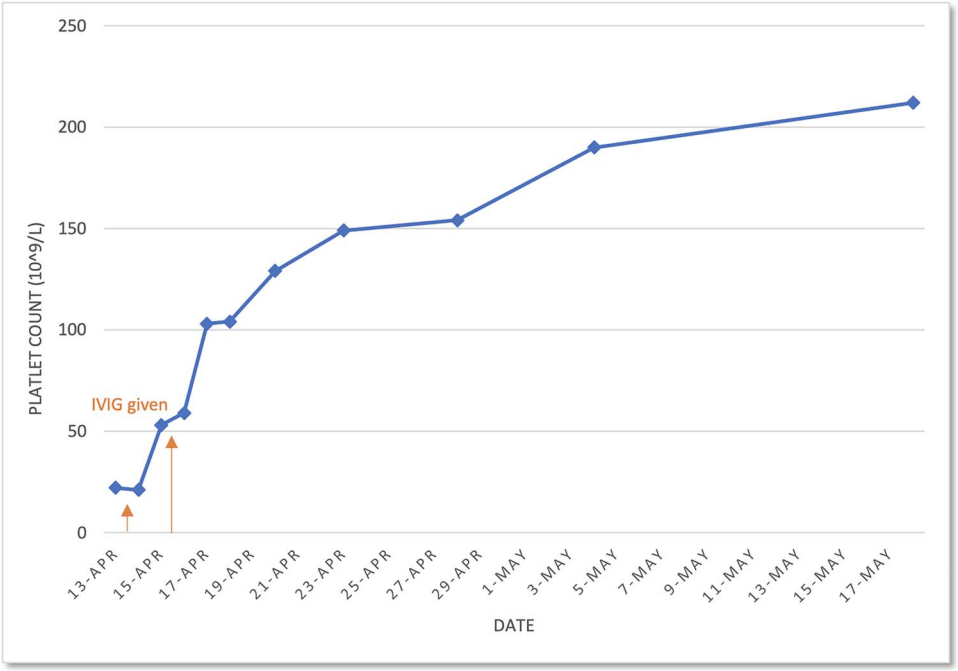

Figure 3. Trend of platelet count after IVIG was given.

family history of venous thromboembolism (VTE) and no recent travel history. She had no evidence of dyslipidaemia and a normal body mass index.

She was referred to secondary care after blood tests revealed a platelet count of 25 × 10^9/l (baseline platelet count was 299 × 10^9/l).

Observations showed a heart rate of 117 beats/minute, apyrexial, saturating 96% on room air. Examination confirmed a lower limb diffuse petechial rash and peripheral bruising.

Significant bloods were a platelet count of 22 109/l (Ref. range: 135–450/l), markedly elevated d-dimer of 23 704 ng/ml (Ref. range: 0–500/l) and a fibrinogen count of 1.5 g/l (Ref. range: 2–4.5 g/l). Enzyme-linked immunosorbent assay confirmed that the patient had antibodies against platelet factor 4 (PF4)-polyanion complexes.

Computed tomography (CT) of head revealed no abnormality, while CT of venogram showed an apparent filling defect extending within the right sigmoid sinus concerning of venous sinus thrombosis with the possibility of arachnoid granulation. Additionally, there were features of idiopathic intracranial hypertension with stenosis of the transverse sinuses bilaterally.

Due to the high suspicion of VITT, intravenous immunoglobulin (IVIG) was commenced at 1 g/kg with a second dose at 0.5 mg/kg and combined with oral prednisolone at 1 mg/kg. Fondaparinux of 2.5 mg OD was started.

She underwent an magnetic resonance imaging (MRI) head and venogram to confirm the CT findings. The initial report concluded that the filling defect noted on CT in the right sigmoid sinus was likely a slight granulation rather than thrombus. However, in view of the clinical suspicion of VITT, a second opinion was sought and the MRV was reported as suggestive of a small-volume venous sinus thrombosis (see Fig. 2). Fondaparinux was increased to 7.5 mg OD.

Due to the rarity of this complication, her case was discussed with a tertiary centre who advised to rule out distant thrombosis.

CTPA confirmed a right-sided subsegmental pulmonary embolus. There was no evidence of mesenteric or portal venous thrombosis. Concurrently, she underwent a ultrasound doppler of her right leg due to swelling, which ruled out a deep vein thrombosis.

Platelet levels began to improve significantly after the second dose of IVIG (see Fig. 3) and her symptoms improved. Fondaparinux was continued (4 days total) until discharge.

She was then started on apixaban 10 mg twice daily for 1 week, which was reduced to 5 mg twice daily, and on a prednisolone weaning regimen. Weekly blood tests showed her platelet counts remained within normal limits and her d-dimer had normalized (d-dimer levels of 23 704–376 after 21 days between 13 April and 11 May). She remains on long-term anticoagulation.

DISCUSSION

This report describes a case of VITT post-administration of the AstraZeneca vaccine in a 55-year-old woman with no history or risk factors for VTE.

This case, as well as other reported incidences, appear to be specific for vaccination. A study in Norway reported that after 132 686 first doses of the AstraZeneca vaccine were administered, five patients were admitted to hospital after 7–10 days after receiving the dose with thrombocytopenia and thrombosis [4]. All five patients had significantly high levels of immunoglobulin G antibodies to PF4 and platelet activation, with no prior exposure to heparin [4].

The association between the AstraZeneca vaccine and the risk of thrombocytopenia and thrombotic events was also assessed in a study using patient level data for ∼29 million people vaccinated in England between 1 December 2020 and 24 April 2021 [5]. An increased risk of thrombocytopenia after the AstraZeneca vaccine and increased risk of VTE and CVST were noted [5].

The features in these cases share similarities with heparin-induced thrombotic thrombocytopenia (HITT). In HITT, platelet-activating antibodies develop after exposure to heparin, which leads to thrombosis and thrombocytopenia [6]. In VITT, it is suspected that cationic PF4 becomes bound with an anionic molecule produced by the cells at the vaccination site or in the vaccine, which then induces antibody formation [6]. These antibodies then bind to platelets via the Fc gamma RIIA receptors which leads to platelet activation, as in HITT [6].

The thrombosis progresses rapidly and has a high disposition at unusual sites, including CVST or the hepatic or portal veins [7]. In previous cases, patients had also presented with DVT, arterial thrombosis and/or pulmonary embolisms [7].

In previous reports of VITT, few patients had a history of thromboembolic events as seen in our case where the patient had no risk factors for VTE and had a low-risk status. Importantly, almost all patients had significant levels of PF4 antibodies [7]. Clinically, the main features seen in these patients present 5–30 days after vaccination and include thrombocytopaenia, thrombosis and raised d-dimer levels [7]. Current diagnostic criteria categorizes patients into unlikely, possible, probable and definite [7].

Anticoagulation is currently the first treatment in probable or definite cases of VITT [8]. IVIG is also used as immunosuppression. After administration, platelet counts rise, and markers of hypercoagulability improve [9]. Studies have shown that serial blood samples obtained in VITT patients before and after two/three doses of IVIG have demonstrated reversion to a weaker or negative PF4-enhanced SRA [9]. Observational data support the concept that high-dose IVIG is effective in VITT [9, 10].

Corticosteroids may be used if IVIG is not available; similar to the management of immune thrombocytopenia (ITP), where corticosteroids are believed to raise the platelet count by decreasing clearance of antibody-coated platelets by macrophages of the reticuloendothelial system [9]. Platelet transfusion was avoided due to the risk of progression of thrombosis [9]. Dose therapy effects in our case was evidenced by improving d-dimer, platelets and fibrinogen.

This case highlights the importance of liaising across specialist centres, which, in our case, advised further imaging to rule out distant thrombosis.

Ultimately, this case highlights the importance of early diagnosis, management and monitoring. Clinicians should be aware of the possibility of VITT after vaccination. As patients with CVST and/or thrombosis due to VITT can become acutely unwell despite initially appearing to be stable, close monitoring is essential.

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CONFLICT OF INTEREST STATEMENT

None declared.

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ETHICAL APPROVAL

No approval was required.

CONSENT

Written consent has been obtained by the patient for this publication.

GUARANTOR

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